

Thrombophilia in Pregnant Women with Gestational Arterial Hypertension and Retinal Vascular Pathology

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Abstract

Research Aim: To study parameters of the hemostatic system, plasma lupus anticoagulant (LA) levels, and hemostasis gene polymorphisms in pregnant women with gestational arterial hypertension (GAH) and retinal vascular pathology.

Materials and Methods: The study included 50 pregnant women aged 22÷37 years at 8÷38 weeks of gestation. Standard and specialized ophthalmological examination methods were used. Hemostasis system studies were performed using screening and specialized methods. Molecular genetic testing was conducted via PCR.

Results and Conclusion: MIT was found in 100% of pregnant women with FPI, GAH, and retinal vascular pathology; LA was present in 16%.

Keywords: Hemostasis System; Pregnant Women; Thrombophilia; LA; Endothelial Dysfunction

Introduction

The urgency of the problem of arterial hypertension and proteinuria in pregnant women, complicated by vascular disorders of the retina and optic nerve, necessitates an in-depth study of the pathogenetic mechanisms of these complications. The purpose of this study was to evaluate changes in hemostasis parameters and levels of lupus anticoagulant (LA) in pregnant women with hypertension and proteinuria complicated by vascular disorders of the retina and optic nerve in order to optimize diagnosis and develop treatment strategies [1,2].

Pregnancy and the postpartum period are states of hypercoagulability with reduced fibrinolytic activity of the blood. During this time, the risk of deep vein thrombosis and pulmonary embolism increases fivefold compared to non-pregnant women of the same age. Women with a history of thrombosis are at increased risk of preeclampsia and fetoplacental insufficiency (FPI) [3,4].

Research Aim

To study parameters of the hemostatic system, plasma lupus anticoagulant (LA) levels, and hemostasis gene polymorphisms in pregnant women with gestational arterial hypertension (GAH) and retinal vascular pathology, fibrinogen gene FGB; prothrombin gene F2, genes of platelet integrin receptors ITGA 2 and ITGB3; P2Y12 ins 801A (AP); gene F5, gene PAI-1, gene F13; genes of the renin-angiotensin system ACE, ATGR1, AGT, gene of endothelial dysfunction NOS3; folate cycle genes (MTHFR C677T, MTHFR methylenetetrahydrofolate reductase); MTHFR A1298C, MTRR.

Materials and Methods

The study included 50 pregnant women aged 22÷37 years at 8÷38 weeks of gestation. Ophthalmological Examinations. Standard examination methods: visual acuity testing, tonometry, perimetry, direct ophthalmoscopy.

Special examination methods: Fundus examination with a Goldman lens, fluorescein angiography (FA) of the fundus, optical coherence tomography (OCT) of the retina, computerized perimetry.

Hemostasis system investigations were conducted using screening and special methods of automated coagulometry: determination of von Willebrand factor (vWF) activity, antithrombin III, activated protein C (APC), factor VIII, quantitative plasma levels of factor V; determination of activated protein C resistance (APCR) or APC resistance index; quantitative determination of soluble fibrin monomer complexes (SFMC); quantitative fibrinogen (by Claus). LA detection was performed using venom tests, as well as confirmatory tests with donor plasma and correcting phospholipids; plasma testing for LA was repeated after 12 weeks. Reference values for LA up to 1.2 u. LA are heterogeneous in their functional properties and, depending on the ability to prolong phospholipid-dependent and phospholipid independent coagulation tests, can be divided into 4 types. LA types 1 and 2 do not have significant thrombogenicity, whereas LA types 3 and 4 are highly thrombogenic.

Reference values for homocysteine in the blood of healthy adults: 5 - 15 $\mu\text{mol/L}$.

Molecular genetic testing using real-time polymerase chain reaction (RT-PCR): F2 gene mutation: 20210G>A; F5 gene mutation: 1691 G>A; FGB gene mutation: -455 G>A; F13A polymorphism; platelet integrin receptor gene polymorphisms: ITGA2: 807 C>T; ITGB3: 1565T>C; plasminogen activator inhibitor-1 (PAI-1): -675 5G>4G; folate gene polymorphisms MTHFR C677T, MTHFR A1298C, MTRR; renin-angiotensin system gene polymorphisms: ACE, ATGR1, AGT; NOS3 gene polymorphism.

Statistical processing of results was performed on a personal computer using the Statistica 6.0 (Statsoft) for Windows application package. Differences were considered statistically significant at a significance level of $p < 0.05$.

Result and Discussion

Multifactorial inherited thrombophilia (MIT) was detected in 100% of pregnant women; LA was found in 16% of cases with FPI. LA significantly reduces endothelial thromboresistance of the retinal microcirculatory bed and enhances hypercoagulation, breaks the natural regulation of the hemostasis system and aggravates retinal ischemia, and is involved in the pathogenesis of acute retinal vascular pathology in pregnant women with GAH. Combination of fibrinogen gene mutations and genes associated with endothelial dysfunction occurred in 40% of cases. In 18% of patients, a combination of prothrombin gene mutation, Leiden mutation, and folate cycle gene

polymorphisms was observed. Polymorphisms in the PAI-1 gene combined with endothelial genes, folate genes, and the P2Y12 gene were present in 20% of cases. Polymorphisms in the F13A gene combined with ITGA2, PAI-1, and folate cycle gene polymorphisms were found in 8% of patients. Factor V Leiden mutation with platelet integrin receptor ITGB3 and ACE, AGT genes occurred in 6% of cases. Factor V Leiden is cleaved more slowly by activated protein C, leading to increased thrombin generation. LA exacerbates endothelial dysfunction in the retinal microcirculation, enhancing thrombogenesis, which clinically manifests as severe retinal thrombohemorrhagic syndrome, diffuse high cystoid macular edema, and retinal ischemia in central and peripheral areas.

Conclusion

MIT was found in 100% of pregnant women with FPI, GAH, and retinal vascular pathology; LA was present in 16%. The combination of hemostasis gene mutations and polymorphisms influences markers of endothelial damage, activating components of the hemostatic system, which clinically manifests as DIC and thrombohemorrhagic syndrome in the retinal microcirculation.

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